## REMARKS

The present paper is responsive to the final Office Action mailed September 26, 2007, and is presented as the necessary submission accompanying a Request for Continued Examination (RCE) under 37 C.F.R. 1.114. Claims 24, 32 and 35 have been amended in this paper. Claims 1-23 and 29-31 are now canceled. Accordingly, claims 24-28 and 32-35 remain pending and the subject of further examination in this application. Specific support for the amendments to claims 24, 32 and 35 is found in the as-filed specification and described in detail below. The amendment enters no new matter in the application.

Each rejection raised by the Examiner is addressed separately below. In view of the claim amendment noted above and the remarks discussed below, Applicants respectfully request reconsideration of the merits of this patent application.

*The Maintained §102(b) Rejection*

In the Office Action mailed September 26, 2007, the Office maintained its rejection of claims 2-3, 5-7, 14-17 and 21-23 under §102(b) as being anticipated by Draber et al. despite Applicants' previous amendments and argument.

Without agreeing to the Office's grounds for rejection and characterization of the art, and solely to move prosecution forward, Applicants have now canceled claims 2-3, 5-7, 14-17 and 21-23 in favor of claims 24-28 and 32-35. However, Applicants reserve the right to pursue any and all subject matter recited in the canceled claims in later filed continuing applications.

Accordingly, Applicants' amendment renders moot the Office's rejection of claims 2-3, 5-7, 14-17 and 21-23 under §102(b).

*The Maintained §103 Rejection*

Claims 2-3, 5-26, 29 and 31- 35 stand rejected under §103 as obvious over Cook et al. (US Patent 6,213,930) in view of Draber et al. and Andya et al.

In light of Applicants' cancellation of claims 2-3, 5-7, 14-17 and 21-23, the present discussion and amendment are directed to remaining claims 24-26, 29 and 31-35.

As amended, claim 24 stands as follows:

Claim 24. A method for producing a feed containing heat-stabilized egg antibodies, the method comprising the steps of:

mixing an egg white, an egg yolk and at least one saccharide selected from a monosaccharide, a disaccharide, a polysaccharide, an alkylated monosaccharide, an alkylated disaccharide, an alkylated polysaccharide, a monosaccharide alcohol, or an alkylated monosaccharide alcohol to form an egg liquid suspension, said egg yolk containing an egg antibody produced in response to antigen inoculation; and

spray drying the egg liquid suspension to form an egg powder; and

processing the egg powder to provide a feed containing heat-stabilized egg antibodies, said processing step including exposing the egg powder to an antigen-binding activity-destroying temperature of at least 70°C;

wherein the heat-stabilized egg antibody in the feed produced by said method loses less of its antigen-binding activity in comparison to an egg yolk antibody provided in a control feed prepared without said saccharide, the heat-stabilized egg antibody retaining at least 20% of its antigen-binding activity after being exposed to said antigen-binding activity-destroying temperature.

Support for the present amendment of claim 24 is provided in the as filed specification at, for example, paragraph [00021], where the steps of heat-stabilizing a protein having a specific binding activity are detailed. Retention of binding activity by heat-stabilized proteins is specifically described with heat-stabilized proteins losing less of their binding activity in comparison to corresponding un-stabilized proteins when exposed to temperatures of at least 70°C. As well, certain embodiments of heat-stabilized proteins are noted as retaining *after* heat exposure at least 20% of binding activity *prior to* heat exposure.

Paragraph [00023] describes mixing egg white, egg yolk and a saccharide followed by spray drying to obtain an egg powder that contains heat-stabilized antibodies. The resulting egg powder is then processed into a feed by a processing method such as, for example, steam pelleting or extrusion. Example 1, provided at paragraphs [00025]-[00028], further describes the production of heat-stabilized egg antibodies via spray drying and steam pelleting methodologies. Accordingly, the subject matter recited in Applicants presently amended claim 24 is supported by the as filed specification and adds no new matter to the respective application.

Dependent claims 30 and 31 have been canceled due to the inclusion of their recited subject matter into independent claim 24. Claims 32 and 35 have been amended to provide proper antecedent basis for certain claimed elements, in view of amended claim 24.

As amended, claim 24 now calls for a method for producing a feed containing heat-stabilized egg antibodies *in which the heat-stabilized egg antibody, upon exposure to an antigen-binding-activity-destroying temperature of at least 70°C during the processing step, loses less of its antigen-binding activity in comparison to an egg yolk antibody provided in a control product prepared without the saccharide addition.* Applicants note that the Office did not direct the present obviousness rejection to dependent claim 30, which previously recited this subject matter and depended from claim 24. The Office will appreciate that the subject matter of claim 30 has now been included in independent claim 24. Accordingly, the cited references, taken alone or in combination, do not teach nor do they suggest the production of feeds containing heat-stabilized egg antibodies in which the heat-stabilized egg antibodies lose less of their antigen-binding activity upon exposure to an antigen-binding activity-destroying temperature of at least 70°C in comparison to an egg yolk antibody provided in a control product prepared without the saccharide addition.

Claims 25, 26, 29 and 31-35, dependent from amended claim 24, recite subject matter which further defines Applicants claimed invention over the cited art. In view of Applicants' amendment and the above discussion, Applicants respectfully request reconsideration of the obviousness rejection and withdrawal of same.

*The New Rejection under §112*

Claims 2-3, 5-7, 12-14 and 16-20 stand rejected under §112, second paragraph, as being indefinite for failing to point out, allegedly, the composition of "steam" recited in those claims, particularly independent claim 14.

Without agreeing to the Office's grounds for rejection, and solely to move prosecution forward, Applicants have now canceled claims 2-3, 5-7, 12-14 and 16-20 in favor of claims 24-28 and 32-35. However, Applicants reserve the right to pursue any and all subject matter recited in the canceled claims in later filed continuing applications.

Accordingly, Applicants' amendment renders moot the Office's rejection of claims 2-3, 5-7, 12-14 and 16-20 under §112, second paragraph.

*The New Rejection under §102(b)*

The Office has rejection of claims 2-3, 5-8, 12-14 and 16-20 under §102(b) as being anticipated by Peebles et al. (U.S. Patent 2,950,204).

Without agreeing to the Office's grounds for rejection and characterization of the art, and solely to move prosecution forward, Applicants have now canceled claims 2-3, 5-8, 12-14 and 16-20 in favor of claims 24-28 and 32-35. However, Applicants reserve the right to pursue any and all subject matter recited in the canceled claims in later filed continuing applications.

Accordingly, Applicants' amendment renders moot the Office's rejection of claims 2-3, 5-8, 12-14 and 16-20 under §102(b).

*The New Rejection under §103*

Claims 24-26 and 29-35 stand rejected under §103 as obvious over Peebles et al. ("Peebles").

As amended, claim 24 now recites a method for producing a feed containing heat-stabilized egg antibodies, the method comprising the steps of: mixing an egg white, an egg yolk and at least one saccharide selected from a monosaccharide, a disaccharide, a polysaccharide, an alkylated monosaccharide, an alkylated disaccharide, an alkylated polysaccharide, a monosaccharide alcohol, or an alkylated monosaccharide alcohol to form an egg liquid

suspension, said egg yolk containing an egg antibody produced in response to antigen inoculation; and spray drying the egg liquid suspension to form an egg powder; and processing the egg powder to provide a feed containing heat-stabilized egg antibodies, said processing step including exposing the egg powder to an antigen-binding activity-destroying temperature of at least 70°C; wherein the heat-stabilized egg antibody in the feed produced by said method loses less of its antigen-binding activity in comparison to an egg yolk antibody provided in a control feed prepared without said saccharide, the heat-stabilized egg antibody retaining at least 20% of its antigen-binding activity after being exposed to said antigen-binding activity-destroying temperature.

The Office alleges that Peebles teach a method of making dried egg products that are suitable in cake mixes. The Office notes at pg. 10 of the Action that Peebles describe:

> "that raw egg white was spray dried to form a good edible dry powdered product. This powdered egg white was then mixed with an equal quantity (by weight) of lactose powder."

In contrast, Applicants' amended claim 24 for preparing a feed containing heat stabilized antibodies includes the distinct steps of:

(1) *mixing an egg white, an egg yolk and at least one saccharide* selected from a monosaccharide, a disaccharide, a polysaccharide, an alkylated monosaccharide, an alkylated disaccharide, an alkylated polysaccharide, a monosaccharide alcohol, or an alkylated monosaccharide alcohol to form an egg liquid suspension, said egg yolk containing an egg antibody produced in response to antigen inoculation;

(2) *spray drying the egg liquid suspension to form an egg powder*; and

(3) *processing the egg powder to provide a feed containing heat-stabilized egg antibodies*, said processing step including exposing the egg powder to an antigen binding-activity-destroying temperature of at least 70°C; wherein the heat-stabilized egg antibody in the feed produced by said method loses less of its antigen-binding activity in comparison to an egg yolk antibody provided in a control feed prepared without said saccharide, the heat-stabilized egg

antibody retaining at least 20% of its antigen binding activity after being exposed to said antigen-binding activity-destroying temperature. (emphasis added)

Applicant wishes to point out that Peebles does not describe *mixing an egg white, an egg yolk and at least one saccharide* prior to *spray drying the egg liquid suspension to form an egg powder*, as explicitly called for in amended claim 24. The mixing of egg white, yolk and saccharide before spray drying is critical to Applicants' claimed invention, as can be appreciated from a review of all general and specific examples provided in the present specification. At paragraphs [0006]-[0007], Applicants describe that saccharide is operably associated with protein molecules to protect the protein's specific binding activity from the destructive effect of processes exposing the protein to heat. Peebles provides no instruction or motivation to alternatively mix the three components prior to a spray drying step nor does Peebles describe or suggest the mechanism of and advantages provided by Applicants order of component addition. In fact, the order of component addition and spray drying described by Peebles would be inoperative in providing Applicants feed containing a heat-stabilized antibody having the heat-resistant and antigen-binding capabilities now explicitly recited in amended claim 24. Simply put, exposing the egg yolk and white to heat before additing the saccharide excipient would provide a product having undesirably reduced heat resistance and antigen-binding capabilities (see, e.g., the results provided at paragraph [00028] of the present specification where comparative data for antigen binding of saccharide protected and unprotected antibodies are discussed and, as well, Example 2 for effects of those antibodies on animal growth).

The Office turns to the KSR court's statements regarding "obvious to try" to provide the necessary rationale for its obviousness rejection. The "problem" facing those in the art, as described by the Office at pg. 11 of the Action, "was to make a mixture of dried egg and lactose, and there was a limited number of methodologies to do so, for example making dried egg and mixing with dried lactose or making a solution of egg and lactose then subsequently drying them by means of spray drying." The Office believes that the artisan would have had reason to try these methodologies with the reasonable expectation that at least one would be successful.

Applicants vigorously disagree with the Office's statement of the problem as it does not fully encompass the actual problem to be solved by the present invention. More specifically, the problem faced by the artisan was to provide a feed containing heat-stabilized egg antibodies

where the egg antibodies are exposed to an antigen-binding activity-destroying temperature of at least 70°C during processing where, despite such exposure, the antibodies lose less antigen-binding activity in comparison to an egg yolk antibody provided in a control feed prepared without a saccharide. Furthermore, amended claim 24 calls for the heat-stabilized antibodies to retain at least 20% of their antigen-binding activity after being exposed to the processing step's antigen-binding activity-destroying temperature.

Peebles simply did not describe nor does it suggest the problem solved by Applicants presently claimed invention. In fact, the Office has provided no references or general teaching in the art at the time of the invention that the problem solved by Applicants currently claimed invention was even recognized in the art. As the problem solved by Applicants claimed invention was not clearly formulated in the art, there could be no identified, predictable solutions available to the artisan at the time of the invention. Without a clear formulation of the problem, the artisan would not have known which options to pursue, and could not have anticipated success or a predictable result.

To further substantiate Applicants position that an artisan would not have predicted the success of the presently claimed invention, Applicant points to various authoritative references describing the high degree of difficulty involved in preparing dried protein formulations which retain biological activity. For example, when salt-free purified albumen was dried using spray versus freeze drying, the changes in the protein were such that functional properties differed (Kitabatake et al., 1989 (attached as Exhibit 1), work also referenced in Abdul-Fattah et al., 2007, first paragraph of introduction, page 1886 (Exhibit 2)). Functional differences noted between samples included differing foam stabilities, intrinsic viscosities, subtilisin acceptabilities, and hydrophobicities (Kitabatake et al., 1989).

Abdul-Fattah et al. (2007), reviews the many outstanding challenges that the pharmaceutical industry faces when trying to dry pure proteins with and without defined excipients. For example, in freeze drying, water is lost as a solid through sublimation, hence it does not act as a solvent or reactant during chemical reactions. The solvent effect of water is critical when spray drying bioactive proteins with carbohydrate excipients since a compositional heterogeneity, with increase bioactive protein at the surface of the molecule, can result, which can dramatically affect the proteins stability in the final product (see Abdul-Fattah et al., 2007,

figure 9, page 1904). Also, differences in stresses such as temperature, shearing, and conditions of dehydration which in turn can effect the structure of the protein, protein aggregation and storage stability vastly differ between the two methods of drying when dealing with pure proteins and defined excipients.

Review of the attached exhibits illustrates that, in particular, it is not obvious to assume that the artisan can maintain the biological activity of a protein, like a spray or freeze dried antibody. Roy and Gupta (2004) (Exhibit 3), an exemplary reference, support this position noting that, with even pure proteins, "seemingly subtle differences in processing conditions can have significant impact on the critical quality attributes of freeze-dried products."

In the specific case of spray drying, since the proteins remain in a liquid solvent (water in the case of eggs), chemical reactions involving proteins such as the Maillard reaction, deamidation, or the oxidation/reduction of disulfide linkages are possible and problematic when attempting to retain biological activity. Antibodies are not exempt from the list of proteins that can be affected by their mixture and handling. In a recent review by Daugherty and Mrsny (2006) (Exhibit 4), depending on formulation and processing of even pure antibodies (even monoclonal antibodies), antibodies are susceptible to oxidation, deamidation, aggregation and fragmentation. "A priori, one might assume that by finding a stable formulation for one of these antibody drugs, that such a formulation would be good for most if not all, similar antibodies. If this were borne out by experience, there would be no need for a review such as this" (Daugherty and Mrsny, 2006, page 690, first paragraph under Section 4. Stability issues for antibody formulations).

The complex mixture of the egg is particularly problematic as the artisan moves from the "gentle" freeze drying method to spray drying. The dehydration of eggs using spray drying has long been known to affect the functionality and solubility of dried egg products (see chapter 13, page 187-196 of Egg Science and Technology W. J. Stadelman and O.J. Cotterill, 2nd edition, 1977) (Exhibit 5). A primary reason for this problem is the interaction of carbohydrates (e. g. glucose, 4% of the albumen) with proteins causing Maillard reactions and/or glucose-cephalin reactions (described on pages 187-188).

Bergquist, at pg. 204 (Exhibit 6), further describes problems associated with retaining the functional properties of dried egg products, particularly yolk-free egg products. Bergquist details

the problems associated with spray drying and notes a variety of attempts to retain the functionality of dried egg products. However, Bergquist does not describe or suggest techniques to retain antigen binding activity of antibodies contained in dried egg products.

In view of the specific knowledge available to the artisan, and the general state of the field, it would have been exceedingly difficult for an artisan to have predicted the results and advantages now offered by Applicants claimed invention. It can be appreciated that the Office's initial statement of the problem faced by the artisan is too superficial, and does not fully encompass the necessity to produce a functional protein, namely, an antibody retaining antigen binding activity. When considered in this fashion, it can be further appreciated that an artisan would have been faced with an extraordinarily large number of solutions, which were largely unpredictable in outcome and therefore offering little to no reasonable expectation of success. As such, the Office's obviousness rejection based on an "obvious to try" rationale is unfounded and should be carefully reconsidered in view of the Applicants present amendment, remarks and supporting exhibits.

Claims 25-26 and 29-35 depend from amended claim 24 and recite additional subject matter which further defines over the cited art. In view of the present amendments and discussion, Applicants respectfully request reconsideration of the outstanding obviousness rejection and withdrawal of same.

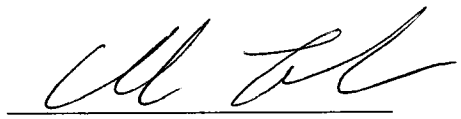
*SUMMARY*

Having addressed each issue raised by the Office, claims 24-28 and 32-35, as amended, are believed to be in condition for allowance and a Notice of Allowance is respectfully requested. Should any issues remain outstanding, the Examiner is invited to contact the undersigned at the telephone number appearing below if such would advance the prosecution of this application.

A Request of Continued Examination (RCE) including the necessary authorization to charge fees accompanies this response along with a petition and authorization to charge for three month extension of time to respond. No other fees are believed to be necessary with the filing of this response. However, if any additional fees or extensions of time are required in this or any subsequent response, please charge the necessary fees and please consider this to be a petition for

the appropriate extension and a request to charge the petition fee to Deposit Account No. 17-0055.

Respectfully submitted,



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